

Z<sub>47</sub> is S or D;  
Z<sub>48</sub> is L or V;  
Z<sub>49</sub> is N or Q;  
Z<sub>50</sub> is V or I; and  
M\* is amino acid 550

*all  
cont.*  
and wherein S\* in Formula I is designated as amino acid 420 and the first S in Formula II is designated as amino acid 421;

and wherein said variants exhibits a replication fitness in the presence of a nucleoside analogue similar to or greater than in the absence of said nucleoside analogue.

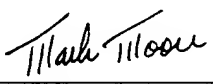
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**REMARKS**

The above amendments are for the purpose of adding the sequence identifier numbers to the specification, drawings and claims. The Examiner is invited to contact the undersigned with any questions or comments.

Respectfully submitted,

Date: November 1, 2001

  
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Mark D. Moore  
Reg. No. 42,903  
WILLIAMS, MORGAN & AMERSON  
7676 Hillmont, Suite 250  
Houston, Texas 77040  
(713) 934-4084  
(713) 934-7011 (facsimile)

AGENT FOR APPLICANTS

**AMENDED CLAIMS FOR APPLICATION SERIAL NO. 09/877,340**

2. (Amended) The HBV variant of claim 1, carrying a mutation in the nucleoside sequence encoding a DNA polymerase resulting in an amino acid addition, substitution and/or deletion in said DNA polymerase in one or more amino acids as set forth in Formula I and/or II:

**FORMULA I**

L, B<sub>1</sub>, B<sub>2</sub>, D, W, G, P, C, B<sub>3</sub>, B<sub>4</sub>, H, G, B<sub>5</sub>, H, B<sub>6</sub>, I, R, B<sub>7</sub>, P, R, T, P, B<sub>8</sub>, R, V, B<sub>9</sub>, G, G, V, F, L, V, D, K, N, P, H, N, T, B<sub>10</sub>, E, S, B<sub>11</sub>, L, B<sub>12</sub>, V, D, F, S, Q, F, S, R, G, B<sub>13</sub>, B<sub>14</sub>, B<sub>15</sub>, V, S, W, P, K, F, A, V, P, N, L, B<sub>16</sub>, S, L, T, N, L, L, S\* (SEQ ID NO:1)

wherein:

- B<sub>1</sub> is L, or R, or I  
B<sub>2</sub> is E, or D  
B<sub>3</sub> is T, or D, or A, or N, or Y  
B<sub>4</sub> is E, or D  
B<sub>5</sub> is E, or K, or Q  
B<sub>6</sub> is H, or R, or N,  
B<sub>7</sub> is I, or T  
B<sub>8</sub> is A, or S  
B<sub>9</sub> is T or R  
B<sub>10</sub> is A, or T, or S  
B<sub>11</sub> is R, or T  
B<sub>12</sub> is V, or G  
B<sub>13</sub> is S, or I, or T, or N, or V  
B<sub>14</sub> is T, or S, or H, or Y  
B<sub>15</sub> is R, or H, or K, or Q  
B<sub>16</sub> is Q, or P;

and

## FORMULA II

S Z<sub>1</sub> L S W L S L D V S A A F Y H Z<sub>2</sub> P L H P A A M P H L L Z<sub>3</sub> G S S G L Z<sub>4</sub> R Y V  
A R L S S Z<sub>5</sub> S Z<sub>6</sub> Z<sub>7</sub> X N Z<sub>8</sub> Q Z<sub>9</sub> Z<sub>10</sub> X X X Z<sub>11</sub> L H Z<sub>12</sub> Z<sub>13</sub> C S R Z<sub>14</sub> L Y V S  
L Z<sub>15</sub> L L Y Z<sub>16</sub> T Z<sub>17</sub> G Z<sub>18</sub> K L H L Z<sub>19</sub> Z<sub>20</sub> H P I Z<sub>21</sub> L G F R K Z<sub>22</sub> P M G Z<sub>23</sub>  
G L S P F L L A Q F T S A I Z<sub>24</sub> Z<sub>25</sub> Z<sub>26</sub> Z<sub>27</sub> Z<sub>28</sub> R A F Z<sub>29</sub> H C Z<sub>30</sub> Z<sub>31</sub> F Z<sub>32</sub> Y  
M\* D D Z<sub>33</sub> V L G A Z<sub>34</sub> Z<sub>35</sub> Z<sub>36</sub> Z<sub>37</sub> H Z<sub>38</sub> E Z<sub>39</sub> L Z<sub>40</sub> Z<sub>41</sub> Z<sub>42</sub> Z<sub>43</sub> Z<sub>44</sub> Z<sub>45</sub> Z<sub>46</sub> L L  
Z<sub>47</sub> Z<sub>48</sub> G I H L N P Z<sub>49</sub> K T K R W G Y S L N F M G Y Z<sub>50</sub> I G (SEQ ID NO:2)

wherein:

- X is any amino acid;
- Z<sub>1</sub> is N or D;
- Z<sub>2</sub> is I or P;
- Z<sub>3</sub> is I or V;
- Z<sub>4</sub> is S or D;
- Z<sub>5</sub> is T or N;
- Z<sub>6</sub> is R or N;
- Z<sub>7</sub> is N or I;
- Z<sub>8</sub> is N or Y or H;
- Z<sub>9</sub> is H or Y;
- Z<sub>10</sub> is G or R;
- Z<sub>11</sub> is D or N;
- Z<sub>12</sub> is D or N;
- Z<sub>13</sub> is S or Y;
- Z<sub>14</sub> is N or Q;
- Z<sub>15</sub> is L or M;
- Z<sub>16</sub> is K or Q;
- Z<sub>17</sub> is Y or F;
- Z<sub>18</sub> is R or W;
- Z<sub>19</sub> is Y or L;

Z<sub>20</sub> is S or A;  
Z<sub>21</sub> is I or V;  
Z<sub>22</sub> is I or L;  
Z<sub>23</sub> is V or G;  
Z<sub>24</sub> is C or L;  
Z<sub>25</sub> is A or S;  
Z<sub>26</sub> is V or M;  
Z<sub>27</sub> is V or T;  
Z<sub>28</sub> is R or C;  
Z<sub>29</sub> is F or P;  
Z<sub>30</sub> is L or V;  
Z<sub>31</sub> is A or V;  
Z<sub>32</sub> is S or A;  
Z<sub>33</sub> is V or L or M;  
Z<sub>34</sub> is K or R;  
Z<sub>35</sub> is S or T;  
Z<sub>36</sub> is V or G;  
Z<sub>37</sub> is Q or E;  
Z<sub>38</sub> is L or S or R;  
Z<sub>39</sub> is S or F;  
Z<sub>40</sub> is F or Y;  
Z<sub>41</sub> is T or A;  
Z<sub>42</sub> is A or S;  
Z<sub>43</sub> is V or I;  
Z<sub>44</sub> is T or C;  
Z<sub>45</sub> is N or S;  
Z<sub>46</sub> is F or V;  
Z<sub>47</sub> is S or D;  
Z<sub>48</sub> is L or V;  
Z<sub>49</sub> is N or Q;  
Z<sub>50</sub> is V or I; and  
M\* is amino acid 550

and wherein S\* in Formula I is designated as amino acid 420 and the first S in Formula II is designated as amino acid 421;

and wherein said variants exhibits a replication fitness in the presence of a nucleoside analogue similar to or greater than in the absence of said nucleoside analogue.